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Septic Arthritis of a Native Knee Joint Due to *Corynebacterium striatum*

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We report a case of septic arthritis of a native knee joint due to *Corynebacterium striatum*, a rare and unusual cause of septic arthritis of native joints. The isolate was identified by a combination of phenotypic, mass spectrometric, and nucleic acid-based assays and exhibited high-level resistance to most antimicrobials.

CASE REPORT

An 84-year-old male with a past medical history of poorly controlled diabetes, coronary artery disease, hypertension, deep vein thrombosis, and anticoagulant use presented with right knee pain and fever. A week prior to admission, he had fallen while trying to climb onto a bus.

Four days prior to admission, a right knee arthrocentesis at his primary care doctor's office, by report, revealed grossly bloody fluid. This was followed by worsening right knee pain upon weight bearing and increasing right knee swelling followed by malaise and subjective fever with chills.

On presentation to the emergency department (ED), he was febrile to 38.5°C. The patient's right lower extremity was edematous, and examination of the right knee revealed minimal erythema, tenderness to palpation, effusion, and a decreased range of motion secondary to pain. In the ED, his knee was aspirated under sterile conditions and yielded 35 ml of straw-colored cloudy fluid. Analysis of the fluid revealed a few calcium pyrophosphate crystals and a white blood cell count elevated to 52,500/μl with 80% neutrophils. A Gram stain of the specimen was negative for organisms. He was empirically started on vancomycin and cefepime and admitted for arthroscopic lavage of the septic knee. He underwent knee lavage in the operating room (OR) 24 h after admission. Two specimens taken from the arthrocentesis procedure in the ED and two from the arthroscopic knee washout in the OR recovered pure cultures of a *Corynebacterium* species. Blood cultures remained sterile after 5 days of incubation.

The patient was maintained on intravenous vancomycin (one gram every 12 h). Cefepime was discontinued, and he completed a 4-week course of vancomycin at a rehabilitation facility. At the completion of the antibiotic course, the patient was followed up by an infectious disease physician and by the orthopedic surgeon. No excess synovial fluid was encountered on a follow-up aspiration of the knee joint, and blood cultures remained sterile.

Three specimens (one taken from the ED and two from the OR) were cultivated on 5% (vol/vol) sheep blood tryptic soy agar plates (Becton, Dickinson and Company, Sparks, MD) incubated at 35°C in 5% carbon dioxide, while one (taken from the ED) was directly inoculated into a blood culture vial (Bactec Plus Aerobic/F culture vial; Becton, Dickinson and Company). All three specimens initially plated to solid media yielded pure cultures of catalase-positive, cream-colored colonies within 48 h, while the blood culture vial was positive within 24 h and, upon subculture, grew a pure culture of catalase-positive, cream-colored organisms. Gram stain of all four isolates revealed pleomorphic, palisading Gram-positive rods.

The isolates were initially identified as *Corynebacterium striatum* with >99% probability using the RapID CB Plus phenotypic system (Remel, Lenexa, KS) (1). Subsequently, the isolates were analyzed by matrix-assisted laser desorption–ionization time of flight mass spectrometry using the recently U.S. Food and Drug Administration (FDA)-cleared Vitek MS v2.0 system (bioMérieux, Durham, NC) (2) and were identified as *C. striatum* with a confidence level of 99.9%. Finally, for one of the isolates, fragments of the 16S rRNA gene (3) and the *rpoB* gene (4) were amplified using the PCR and the PCR products sequenced. However, although they are highly accurate for bacterial identification, neither of these sequence-based methodologies is cleared by the FDA for bacterial identification and both remain restricted to research use only.

The resultant 16S rRNA gene sequence data were analyzed using SmartGene IDNS (Integrated Database Network System) software (SmartGene GmbS, Lausanne, Switzerland) (5), and the results revealed that the best match was *C. striatum* type strain ATCC 6940, with 99.6% similarity (470 bp/472 bp), while the next-best match was *C. xerosis*, with 98.9% similarity (467 bp/472 bp). According to the standards adopted by the Clinical Laboratories Standards Institute (CLSI), the 16S rRNA gene sequence analysis satisfied genus-level but not species-level identification

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requirements (6). The *rpoB* gene sequence data were queried against GenBank (http://www.ncbi.nlm.nih.gov) and the European Nucleotide Archive (ENA; http://www.ebi.ac.uk/ena/). The best match returned from GenBank was *C. striatum* type strain CIP 81.15, with 97.3% similarity (434 bp/446 bp), while the next-best match was *C. simulans* type strain CIP 106488, with 94.0% similarity (419 bp/446 bp). The ENA returned a best match of *C. striatum* type strains 6940 and CIP 81.15, both with 97.3% similarity (434 bp/446 bp). The next-best match was *C. simulans* type strain CIP 106488, with 94.0% similarity (419 bp/446 bp). Taken together, the 16S rRNA gene and *rpoB* gene sequence data strongly support the phenotypic and mass spectrometric identification of *C. striatum*.

Antimicrobial susceptibility testing results for all four isolates were determined using an Etest (bioMérieux) method that was verified against the published CLSI test conditions (7). A 0.5 McFarland standard was prepared and cultured on Mueller-Hinton agar supplemented with 5% (vol/vol) sheep blood (Remel) for 48 h. Using breakpoints established by the CLSI (7), Etest values revealed that all four isolates were resistant to clindamycin, ciprofloxacin, tetracycline, and ceftriaxone, with MIC values $>$ 256 μg/ml, while all four isolates were susceptible to vancomycin (MIC of 1 μg/ml).

Corynebacterium species are opportunistic human pathogens, and due to their association with skin and mucous membranes in asymptomatic individuals, these organisms are often considered contaminants when isolated in culture (8). However, when isolated repeatedly in pure growth from a normally sterile body site, e.g., synovial fluid or blood, in a clinical context consistent with infection, they should be considered clinically relevant and identification to the species level and antimicrobial susceptibility testing is recommended (8).

C. striatum has been associated with invasive infections, including infective endocarditis, pulmonary infections, and prosthetic joint infections (9–12). However, to the best of our knowledge, there are only four cases in the published literature describing septic arthritis of native joints due to *C. striatum* (PubMed [http://www.ncbi.nlm.nih.gov/pubmed]; terms "corynebacterium," "striatum," "septic," and "arthritis") (11, 13–15), including two cases of septic arthritis of the shoulder (11, 15), one case of a septic elbow (13), and one case of septic arthritis of the knee (14). Thus, as far as we are aware, the case presented here is only the second case of septic arthritis of a native knee joint due to *C. striatum*.

The report of a previous case of native knee septic arthritis describes an 87-year-old male with a history of osteoarthritis and advanced heart failure who, following a fall, presented with a swollen knee (14). Aspirated synovial fluid revealed inflammatory cells without crystals, and both synovial fluid and blood cultures were negative. Approximately 3 weeks later, he returned with pneumonia due to *Streptococcus pneumoniae* and an inability to bear weight. Again, aspirated synovial fluid revealed inflammatory cells without crystals; however, upon two occasions *C. striatum* was recovered in pure culture within 24 h of culture inoculation. Interestingly, rather than attributing the infection due to direct inoculation of skin-associated *C. striatum* during aspiration of the joint, it was suggested that the infection was spontaneous and that the offending *C. striatum* isolate gained access to the patient's circulation either during the episode of pneumonia or through open venous stasis ulcers.

There are significant similarities between our case and the aforementioned case, namely, the blunt trauma of the knee prior to presentation and the underlying immunosuppression associated with the patients. However, rather than interpreting ours as a second case of spontaneous infection of a joint due to *C. striatum*, we believe that iatrogenic inoculation of the joint with skin-associated *C. striatum* during the first knee aspiration likely resulted in the infection described in our case.

The identification of *Corynebacterium* species to the species level is often difficult or unreliable if phenotypic testing is the sole identification method utilized (8, 9). Therefore, to confirm the phenotypic identification of *C. striatum*, we utilized mass spectrometric and nucleic acid-based methodologies, with both methodologies convincingly identifying the isolates as *C. striatum*. Mass spectrometric identification of microbes, including *Corynebacterium* species, is revolutionizing the fields of clinical microbiology and infectious diseases and has the ability to rapidly identify *Corynebacterium* species to a level comparable to that achievable with the more labor-, time-, and cost-intensive sequence-based methods (16).

Antimicrobial susceptibility testing of *Corynebacterium* species should be performed if the isolate is considered clinically relevant, as antimicrobial susceptibility is not predictable on the basis of genus- and species-level identification (8). This is partially due to the fact that, historically, many laboratories were unable to reliably identify coryneform bacteria to the species level. Further, *Corynebacterium* species, especially *C. striatum*, demonstrating multidrug resistance have been recovered from clinical specimens, with isolates displaying resistance to several classes of antimicrobials, including beta-lactams, fluoroquinolones, macrolides, lincosamides, and tetracyclines. Typically, these multidrug-resistant isolates are susceptible only to vancomycin, daptomycin, and linezolid (8, 14). The isolates obtained from our patient were multidrug resistant; of all the antimicrobials assayed, vancomycin was the only antimicrobial that tested as susceptible.

This case further highlights the role of *C. striatum* in native joint infections. Additionally, it emphasizes the importance of identifying *Corynebacterium* species isolates recovered in multiple cultures to the species level and performing antimicrobial susceptibility testing due to the increased frequency of multidrug resistance in this genus.

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REFERENCES

1. **Funke G, Peters K, Aravena-Roman M.** 1998. Evaluation of the RapID CB Plus system for identification of coryneform bacteria and *Listeria* spp. J. Clin. Microbiol. **36:**2439–2442.
2. **Rychert J, Burnham C-AD, Bythrow M, Garner OB, Ginocchio CC, Jennemann R, Lewinski MA, Manji R, Mochon AB, Procop GW, Richter SS, Sercia L, Westblade LF, Ferraro MJ, Branda JA.** 2013. Multicenter evaluation of the Vitek MS matrix-assisted laser desorption ionization-time of flight mass spectrometry system for identification of

gram-positive aerobic bacteria. J. Clin. Microbiol. **51:**2225–2231. http://dx.doi.org/10.1128/JCM.00682-13.
3. **Kommedal Ø, Simmon K, Karaca D, Langeland N, Wiker HG.** 2012. Dual priming oligonucleotides for broad-range amplification of the bacterial 16S rRNA gene directly from human clinical specimens. J. Clin. Microbiol. **50:**1289–1294. http://dx.doi.org/10.1128/JCM.06269-11.
4. **Khamis A, Raoult D, La Scola B.** 2004. *rpoB* gene sequencing for identification of *Corynebacterium* species. J. Clin. Microbiol. **42:**3925–3931. http://dx.doi.org/10.1128/JCM.42.9.3925-3931.2004.
5. **Simmon KE, Croft AC, Petti CA.** 2006. Application of SmartGene IDNS software to partial 16S rRNA gene sequences for a diverse group of bacteria in a clinical laboratory. J. Clin. Microbiol. **44:**4400–4406. http://dx.doi.org/10.1128/JCM.01364-06.
6. **Clinical and Laboratory Standards Institute.** 2008. Interpretative criteria for identification of bacteria and fungi by DNA target sequencing; approved guideline. MM18-A, vol 28. Clinical and Laboratory Standards Institute, Wayne, PA.
7. **Clinical and Laboratory Standards Institute.** 2010. Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria; approved guideline—second edition. M45-A2, vol 30. Clinical and Laboratory Standards Institute, Wayne, PA.
8. **Bernard K.** 2012. The genus *Corynebacterium* and other medically relevant coryneform-like bacteria. J. Clin. Microbiol. **50:**3152–3158. http://dx.doi.org/10.1128/JCM.00796-12.
9. **Roux V, Drancourt M, Stein A, Riegel P, Raoult D, La Scola B.** 2004. *Corynebacterium* species isolated from bone and joint infections identified by 16S rRNA gene sequence analysis. J. Clin. Microbiol. **42:**2231–2233. http://dx.doi.org/10.1128/JCM.42.5.2231-2233.2004.
10. **Renom F, Garau M, Rubí M, Ramis F, Galmés A, Soriano JB.** 2007. Nosocomial outbreak of *Corynebacterium striatum* infection in patients with chronic obstructive pulmonary disease. J. Clin. Microbiol. **45:**2064–2067. http://dx.doi.org/10.1128/JCM.00152-07.
11. **Boltin D, Katzir M, Bugoslavsky V, Yalashvili I, Brosh-Nissimov T, Fried M, Elkayam O.** 2009. *Corynebacterium striatum* - a classic pathogen eluding diagnosis. Eur. J. Intern. Med. **20:**e49–e52. http://dx.doi.org/10.1016/j.ejim.2008.08.009.
12. **Cazanave C, Greenwood-Quaintance KE, Hanssen AD, Patel R.** 2012. *Corynebacterium* prosthetic joint infection. J. Clin. Microbiol. **50:**1518–1523. http://dx.doi.org/10.1128/JCM.06439-11.
13. **Cone LA, Curry N, Wuestoff MA, O'Connell SJ, Feller JF.** 1998. Septic synovitis and arthritis due to *Corynebacterium striatum* following an accidental scalpel injury. Clin. Infect. Dis. **27:**1532–1533. http://dx.doi.org/10.1086/517737.
14. **Scholle D.** 2007. A spontaneous joint infection with *Corynebacterium striatum*. J. Clin. Microbiol. **45:**656–658. http://dx.doi.org/10.1128/JCM.00827-06.
15. **Feced Olmos CM, Alegre Sancho JJ, Ivorra Cortés J, Román Ivorra JA.** 2013. Septic arthritis of the shoulder due to *Corynebacterium striatum*. Reumatol. Clin. **9:**383. http://dx.doi.org/10.1016/j.reuma.2013.02.006.
16. **Alatoom AA, Cazanave CJ, Cunningham SA, Ihde SM, Patel R.** 2012. Identification of non-*diphtheriae Corynebacterium* by use of matrix-assisted laser desorption ionization–time of flight mass spectrometry. J. Clin. Microbiol. **50:**160–163. http://dx.doi.org/10.1128/JCM.05889-11.